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Published in:
Danish Medical Journal

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Citation for pulished version (APA):
Pedersen, B., Ellebæk, M. B., Dorfelt, A., & Qvist, N. (2017). Cholecystectomy for uncomplicated gallbladder stones does not follow evidence-based recommendations. Danish Medical Journal, 64(11), [A5411].

Cholecystectomy for uncomplicated gallbladder stones does not follow evidence-based recommendations

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ABSTRACT

INTRODUCTION: The introduction of laparoscopic cholecystectomy was followed by a steep increase in the cholecystectomy rate, which has remained on an unchanged, high level. The main indication for cholecystectomy in Denmark in cases with uncomplicated gallbladder stones is socially debilitating pain. The objective of the present study was to investigate whether the indication "socially debilitating pain" was reported in the patient's file when he or she was referred to surgery.

METHODS: Hospital files for all patients referred to surgical evaluation for uncomplicated gallbladder stones from Odense University Hospital's service area (approximately 449,000 inhabitants) within a one-year period (2014) were reviewed.

RESULTS: Among 1,003 eligible patients, a total of 516 met the inclusion criteria, 407 (78.9%) of whom underwent elective cholecystectomy. For only 89 (21.9%) of these 407 patients, the indication of socially debilitating pain was described in the patient files.

CONCLUSIONS: Our results may represent overtreatment and/or incorrect selection of patients suitable for surgery. More and larger prospective cohort studies are warranted to elucidate the indications for cholecystectomy in uncomplicated gallbladder stones.

FUNDING: none.

TRIAL REGISTRATION: not relevant.

Asymptomatic ("silent") gallbladder stones are common in the general population with a reported prevalence up to 22.4% [1, 2]. Within a 20-year observation period, up to 18% of these citizens will experience symptoms in the form of recurrent abdominal pain, nausea and food intolerance or undergo cholecystectomy due to symptoms, and up to 8% will develop complications (choledocolithiasis, cholecystitis, cholangitis or pancreatitis) [3].

According to national guidelines, laparoscopic cholecystectomy is currently considered the gold standard for treatment of symptomatic gallbladder stones [4, 5]. However, studies have shown that up to 2% of the patients who undergo laparoscopic cholecystectomy will experience complications to some extent, and up to 0.63% will suffer from severe complications like bile leak or bile duct injuries, which is associated with great morbidity and even with mortality [6]. Furthermore, after cholecystectomy for uncomplicated gallbladder stones, 4-47% will experience persistent abdominal symptoms (post-cholecystectomy syndrome) depending on the patient selection [7, 8]. Therefore, conservative treatment with watchful waiting might be a preferable alternative to operation in cases with mild or rare symptoms. A large cohort study by Shabanzadeh DM et al found that epigastrial pain, hours of pain duration and need of pain medication were correlated to later events/complications and that these factors may guide patients and physicians in the choice between cholecystectomy or watchful waiting [9].

In Denmark, the number of cholecystectomies increased from approximately 67 operations per 100,000 inhabitants in 1989 to 143 operations per 100,000 inhabitants in 2003 [10]. The introduction of laparoscopic surgery and/or an increased demand for operation among patients might be the explanation [1, 10]. On this background, the Danish Health Authority released an evidence-based recommendation stating that the main indication for cholecystectomy in uncomplicated cases with gallbladder stones should be socially debilitating pain, which by nature is very dependent on individual circumstances [4]. Following this new recommendation, one would expect the cholecystectomy rate to decrease, but in 2014 we carried out 138 operations per 100,000 inhabitants [11] leaving the cholecystectomy rate on an unchanged high level for more than a decade. The same trend has been observed in Sweden with a slight decrease from 161 operations per 100,000 inhabitants in 1998 to 137 per 100,000 inhabitants in 2013 [12].

The objective of the present study was to investigate whether the indication "socially debilitating pain" was reported in the patient's file when he or she was referred to surgery. Our hypothesis was that socially debilitating pain as an indication for cholecystectomy was not well described or defined in the patient records and that only a minority of patients were referred for conservative treatment.

ORIGINAL ARTICLE

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Dan Med J 2017;64(11):A5411

METHODS

Patients

We reviewed files for patients above 15 years of age who were referred to surgical evaluation for uncomplicated gallbladder stones within Odense University Hospital's service area (approximately 449,000 inhabitants) in Denmark from 1 January to 31 December 2014. Patients were identified in the hospital's electronic case record system using The International Classification of Diseases (ICD)-10 by searching for the following codes: DK80, DK802, DK802A, DK802D-F, DK805, DK805J-K and DK808. Each patient file was reviewed for specific data regarding demographics, clinical symptoms, patient preference for treatment, actual treatment, earlier hospital admissions, diagnostic tool, comorbidity, biochemistry and finally whether "debilitating pain" was described.

The Danish Patient Safety Authority (file no: 3-3013-1705/1/) and The Danish Data Protection Agency (file no: 16/18475) approved the project prior to data collection, and OPEN Redcap was used as the study database.

Inclusion and exclusion criteria

We defined uncomplicated gallbladder stones as follows: Patients with verified gallstone(s) (ultrasonic (UL) or by magnetic resonance imaging (MRI)/computed tomography (CT)), who were referred to hospital for evaluation of abdominal pain with or without dyspeptic symptoms. All patients with clinical, biochemical or radiographic signs of gallbladder inflammation, obstruction of bile ducts, malignancy or other abdominal abnormalities were excluded (**Table 1**).

TABLE 1

Eligible patients and the reasons for exclusion. The values are n (%).

Included	516 (51.4)
Excluded	487 (48.6)
Cholecystitis: earlier/current	134 (13.4)
Choledocolithiasis: earlier/current	94 (9.4)
Referred to another region or private hospital	48 (4.8)
Never evaluated by sugeon	35 (3.5)
Pancreatitis caused by gallstone	30 (3.0)
Gall bladder polyps with 0 stones	26 (2.6)
Wrong ICD-10 code	20 (2.0)
Jaundice: earlier/current	19 (1.9)
Had cholecystectomy before 2014	15 (1.5)
0 gall bladder stones: UL/MRI/CT	15 (1.5)
Cholangitis: earlier/current	14 (1.4)
Other reasons	9 (0.9)
Suspicion of cholangiocarcinoma/pancreas cancer	8 (0.8)
Suspicion of choledocolithiasis	6 (0.6)
< 15-yr-old	4 (0.4)
Medical induced effect on liver	3 (0.3)
Patients preference due to comorbidity	2 (0.2)
Stenosis in biliary system	2 (0.2)
Internal herniation	2 (0.2)
Patient died before surgical evaluation	1 (0.1)
Patients, total	1,003 (100.0)

CT = computed tomography; ICD = International Classification of Disease; MRI = magnetic resonance imaging; UL = ultrasonic.

Definition of "socially debilitating pain"

To ensure consistency throughout the data collection, we agreed on defining socially debilitating pain as any description that considered the influence of the symptoms on the patient's life. This could be regarding work, e.g. sick leave, social skills, e.g. unable to perform daily activities, psychological, e.g. anxiety for new attacks of pain or if the patient felt the situation was unsustainable. Consequently, all files only describing symptoms in an objective/quantitative manner were categorised as non-debilitating pain.

Statistics

Statistical analysis was preformed using STATA 14.0. For categorical data, we used Pearson's chi squared test unless the variables were small (< 10), in which case we used Fisher's exact test. For continuous data that were normally distributed, we used Student's t-test. Data with a non-normal distribution were tested by a non-parametric k-sample test on the equality of medians. A p-value < 0.05 was considered statistically significant.

Trial registration: not relevant.

RESULTS

Overall demographics for included patients

Of the 1,003 patients referred to surgical evaluation in the observation period, 516 met the inclusion criteria. The female:male ratio was 4:1. The mean age was 48 years and the mean body mass index (BMI) was 29. In 422 patients, gallstone was verified by UL, 31 were verified by MRI, 15 by CT and 48 had unknown diagnostic imaging because the diagnostic procedures had been performed outside of our region.

Surgery versus watchful waiting

A total of 407 (78.9%) of the included 516 patients underwent elective cholecystectomy. Those who underwent cholecystectomy were significantly younger than those who did not with a mean age of 46 and 56, respectively ($p < 0.001$). There was no significant difference between the two groups regarding sex or BMI. In the group of patients who underwent cholecystectomy (surgery group (SG)) significantly more reported symptoms once/week or more often and with a duration of more than three months than in the watchful waiting

group (WW). The values were 44.5% versus 16.5% (p = 0.001) and 59.5% versus 47.7% (p = 0.03), respectively (**Table 2**). In both groups, pain was most often located under the right costal margin (68.6% for SG versus 58.7% for WW) followed by "atypical pain location" (35.6% versus 37.6%) and epigastric pain (23.6% versus 18.3%). Socially debilitating pain was more often described in the SG and more patients had a preference for surgery than in the WW (21.9% versus 4.6%; p < 0.001) and (35.1% versus 4.6%; p < 0.001), respectively. As to hospital admissions caused by gallbladder stones prior to surgical evaluation, both the number of patients and the mean number of admissions per patient in the SG was higher than in the WW. The numbers being 80 versus 11 and 0.28 versus 0.11 (p = 0.02 for both), respectively (Table 2).

In the WW group, more patients had bilirubin and alkaline phosphatase (ALP) levels above the reference value than in the SG, 20.2% versus 12.5% (p = 0.042) and 34.9% versus 21.9% (p = 0.005), respectively (Table 2). Also, patients in the WW had a higher frequency of hypertension, diabetes and ischaemic heart disease, 28.4% versus 20.6% (p = 0.002), 8.3% versus 4.7% (p = 0.039) and 16.5% versus 7.4% (p < 0.001), respectively. More patients in the SG had previous abdominal surgery than in the WW (38.3% versus 19.3%; p = 0.007). American Society of Anesthesiologists (ASA)-scores 1 and 2 were more frequent for patients in the SG: 47.9% versus 9.2% and 40.8% versus 14.7% (p = 0.007), for both. While ASA-score 3 was more frequent in the WW group (4.6% versus 2.9%; p = 0.007) (Table 2).

Socially debilitating pain

Of the 407 patients who underwent cholecystectomy, only 89 (21.9%) had debilitating pain described in their files, and of these 89 patients more had experienced symptoms for longer than three months compared with the group without this description (69.7% versus 56.6%; p = 0.027) (**Table 3**). In the group without a description of debilitating pain, more patients had a history of previous abdominal surgery (29.2% versus 40.9%; p = 0.045) (Table 3). All other variables were similar in the two groups (Table 3).

DISCUSSION

Indication for surgery

The majority of patients (78.9%) who were referred to hospital for uncomplicated gallbladder stones were subsequently referred for a cholecystectomy. Only 21.9% of these patients had the indication "socially debilitating pain" described in their files, which should be the main indication according to national recommendations. However, significantly more patients in the SG had a history of more frequent symptoms and longer symptom

TABLE 2

Comparison of patients who underwent cholecystectomy versus being referred to watchful waiting.

	Surgery (N = 407)	Watchful waiting (N = 109)	p-value
Frequency of symptoms within last 3 mo.s, n (%)			
≤ once/wk	104 (25.55)	42 (38.53)	< 0.001
> once/wk	181 (44.47)	18 (16.51)	
Unknown	122 (29.98)	49 (44.95)	–
Overall duration of symptoms, n (%)			
≤ 3 mo.s	77 (18.92)	27 (24.77)	
> 3-6 mo.s	60 (14.74)	7 (6.42)	0.102
> 6 mo.s-1 yr	51 (12.53)	12 (11.01)	
> 1 yr	131 (32.19)	33 (30.28)	
> 3 mo.s, total	242 (59.46)	52 (47.71)	0.028
Unknown	88 (21.62)	30 (27.52)	–
Location of pain, n (%)			
Epigastric	96 (23.6)	20 (18.3)	0.245
Right costal margin	279 (68.6)	64 (58.7)	0.053
Right flank	7 (1.7)	1 (0.9)	1
Atypical localization	145 (35.6)	41 (37.6)	0.701
Unknown	4 (1.0)	5 (4.6)	–
Debilitating pain described in file, n (%)	89 (21.87)	5 (4.59)	< 0.001
Patient preference, n (%)			
Operation	143 (35.14)	5 (4.59)	< 0.001
Watchful waiting	0	32 (29.36)	
Unknown	264 (64.86)	72 (66.06)	–
Admissions			
Patients with earlier hospital admission, n (%)	80 (19.66)	11 (10.09)	0.02
Admissions, total, n	115	12	–
Admissions/patient, n, mean (range)	0.28 (0-4)	0.11 (0-2)	0.02
Biochemistry, n [missing] (%)			
Patients with bilirubin level > 25 µmol/l	51 [42] (12.53)	22 [20] (20.18)	0.042
Patients with alkaline phosphatase level > 105 U/l	89 [40] (21.87)	38 [15] (34.86)	0.005
Patients with alanine aminotransferase level > 45 U/l	116 [37] (28.50)	35 [15] (32.11)	0.462
Previous abdominal surgery, n (%)			
Yes	156 (38.33)	21 (19.27)	0.007
No	251 (61.67)	69 (63.30)	
Unknown	0	19 (17.43)	–
Comorbidity, n (%)			
Hypertension	84 (20.64)	31 (28.44)	0.002
Diabetes	19 (4.67)	9 (8.26)	0.039
Ischaemic heart disease	30 (7.37)	18 (16.51)	< 0.001
Pulmonary disease	29 (7.13)	7 (6.42)	0.653
Kidney disease	2 (0.49)	0	1
Liver disease	1 (0.25)	0	1
ASA-score, n (%)			
1	195 (47.91)	10 (9.17)	0.007
2	166 (40.79)	16 (14.68)	
3	12 (2.95)	5 (4.59)	
4	1 (0.25)	0	
Unknown	33 (8.11)	78 (71.56)	–

ASA = American Society of Anesthesiologists.

TABLE 3

Comparison of all patients who underwent cholecystectomy as to whether they had debilitating pain described in their file.

	Debilitating pain		
	described (N = 89)	not described (N = 318)	p-value
Frequency of symptoms within last 3 mo.s, n (%)			
≤ once/wk	19 (21.35)	85 (26.73)	0.076
> once/wk	50 (56.18)	131 (41.19)	
Unknown	20 (22.47)	102 (32.08)	–
Overall duration of symptoms, n (%)			
≤ 3 mo.s	17 (19.10)	60 (18.87)	
> 3-6 mo.s	19 (21.35)	41 (12.89)	0.581
> 6 mo.s-1 yr	12 (13.48)	39 (12.26)	
> 1 yr	31 (34.83)	100 (31.45)	
> 3 mo.s, total	62 (69.66)	180 (56.60)	0.027
Unknown	10 (11.24)	78 (24.53)	–
Location of pain, n (%)			
Epigastric	19 (21.35)	77 (24.21)	0.574
Right costal margin	63 (70.79)	216 (67.92)	0.607
Right flank	2 (2.25)	5 (1.57)	0.65
Atypical localization	34 (38.20)	111 (34.91)	0.566
Unknown	0	4 (1.26)	–
Patient preference, n (%)			
Operation	36 (40.45)	107 (33.65)	0.235
Unknown	53 (59.55)	211 (66.35)	
Admissions			
Patients with earlier hospital admission, n (%)	17 (19.10)	63 (19.81)	0.882
Admissions, total, n	25	90	–
Admissions/patient, n, mean (range)	0.28 (0-4)	0.28 (0-5)	0.882
Biochemistry, n [missing] (%)			
Patients with bilirubin level > 25 µmol/l	11 [10] (12.36)	40 [32] (12.58)	0.956
Patients with alkaline phosphatase level > 105 U/l	20 [11] (22.47)	69 [29] (21.70)	0.876
Patients with alanine aminotransferase level > 45 U/l	27 [10] (30.34)	89 [27] (27.99)	0.664
Previous abdominal surgery, n (%)			
Yes	26 (29.21)	130 (40.88)	0.045
No	63 (70.79)	188 (59.12)	
Comorbidity, n (%)			
Hypertension	14 (15.73)	70 (22.01)	0.196
Diabetes	5 (5.62)	14 (4.40)	0.579
Ischaemic heart disease	6 (6.74)	24 (7.55)	1.000
Pulmonary disease	4 (4.49)	25 (7.86)	0.355
Kidney disease	1 (1.12)	1 (0.31)	0.39
Liver disease	1 (1.12)	0	0.219
ASA-score, n (%)			
1	49 (55.06)	146 (45.91)	
2	31 (34.83)	135 (42.45)	0.33
3	1 (1.12)	11 (3.46)	
4	0	1 (0.31)	
Unknown	8 (8.99)	25 (7.86)	–

ASA = American Society of Anesthesiologists.

duration. In addition, they had a higher rate of previous hospital admissions due to gallbladder stones and a higher preference for surgery. On the other hand, WW patients tended to be frailer with a higher frequency of comorbidities; hypertension, diabetes and ischaemic heart disease and they were, on average, ten years older than the SG patients, which may explain the choice of conservative treatment. This information may indicate that other indications might have played an important role in selecting patients for surgery or watchful waiting. Due to missing data in the WW, it is difficult to draw any final conclusions from ASA scores and previous abdominal surgery, and there is no obvious explanation for the fact that more patients on watchful waiting had elevated levels of bilirubin and ALP compared with the surgery group.

The explanation for patients being referred to cholecystectomy without the proper indication of socially debilitating pain described in their files cannot be discerned from the present study. That some patients with a preference for surgery had their desire met by the surgeon could explain some of the cases, but this explanation will hardly account for them all. Similarly, we cannot determine what caused a persistent high cholecystectomy rate after the new recommendations were released in 2006, but it might be an expression of the prolonged process needed to implement new evidence in clinical practice.

That patients are being referred for cholecystectomy without the proper indication could have extensive consequences for the patient and for society. The frequency of serious complications to cholecystectomy are not negligible, but have to be weighed against the fact that up to 8% of patients will, over time, develop complications to gallbladder stones when treated conservatively [3]. It is noteworthy that we still do not know who will benefit most from surgery or from watchful waiting [13]. The problem with patient selection for cholecystectomy seems to be relevant worldwide. Though several countries have their own guidelines, Van Dijk et al found that many of these are not suitable for clinical practice, either because of a low level of evidence or due to a lack of consensus [14]. Thus, a great variation in the cholecystectomy rate within the Scandinavian countries has been reported, with markedly higher rates in Finland and Sweden even though the highest prevalence of gallstones has been observed in Norway [15].

Strengths and limitations

The present study faces the same limitations as most retrospective studies in its inability to trail important data if these are missing. Consequently, we had to define a very rigid and simple definition of "socially debilitating pain". This is problematic and our definition might be unprecise or even incorrect. Also, our results are very dependent on the patients' records, which could be incomplete. Therefore, the present study cannot determine whether the indication for cholecystectomy was

too liberal or not, or whether the patients benefited from the decision made with respect to surgery or watchful waiting. Only large prospective trials with well-defined indications for cholecystectomy may provide this answer. A minority of the included patients was submitted to the emergency department because of abdominal pain, which might influence the routine setting for evaluation for surgery and thereby cause bias favouring surgery.

For patients who were selected for conservative treatment, there were often missing data because their personal records were not as complete as those of patients who were referred for surgery. Therefore, it was difficult to make final conclusions between the two groups for some variables, e.g. ASA score, even though we found a statistically significant difference. Throughout the statistical work, the variable "unknown" representing missing data was omitted to minimise the risk of bias, but this is still problematic and any interpretation of our results should be made with caution – especially when the size of "unknown" data is unequal between two groups. Also, some of the variables/events only occurred a few times within our population, leaving small data amounts for statistical analysis.

The strengths of the present study are that all eligible cases from a well-defined catchment area were included within a continuum of one year. Furthermore, all files were reviewed by a single researcher to ensure a consistent interpretation of the data throughout the entire data collection.

CONCLUSIONS

For more than three quarters of the patients with uncomplicated gallbladder stones referred for cholecystectomy, the generally accepted main indication of socially debilitating pain was not described in medical files. This is problematic and could lead to overtreatment and/or incorrect selection of patients suitable for surgery. More and larger prospective studies are warranted to explore this topic.

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ACCEPTED: 28 August 2017

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

ACKNOWLEDGEMENTS: The authors take this opportunity to express their gratitude to *Sören Möller* and *Lars Søgaard* from OPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark, for their assistance with data processing and database design, respectively.

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